Poly(ethylene glycol) as an Electron-Beam Resist to Control Protein Adsorption and Cell Adhesion

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Statement of Purpose: Precise micro/nano-structured features developed using electron-beam patterning has been widely used to control the surface interactions with biological systems. –Here we explore the properties of Poly(ethylene glycol) (PEG) as negative electron beam resist for biointeractive applications, particularly as a means to spatially control protein adsorption. PEG in various forms – e.g. as bulk gels, thin films, self-assembled monolayers - has been used extensively to resist protein and cell adhesion. Much of this has been done using laterally continuous PEGylation. Recent work has concentrated on laterally modulating protein and cell adhesiveness to surfaces. Via e-beam patterning we can precisely control PEG gel size, swell properties, and spatially distribution on a surface and thus to control the spatial distribution of protein adsorption, and hence the subsequent adhesion of bacteria and/or tissue cells, with sub-micron precision.

Methods: Electron-beam patterning was performed in a FEI Helios scanning electron microscope, controlled by a Nabity Pattern Generation System (NPGS), located within the Center for Functional Nanomaterials (CFN) at Brookhaven National Laboratory. PEG gels were cross-linked onto glass surfaces using incident electron energies ranging from 2- 30 keV and doses ranging from 0.005-1000 fC per exposure point. As illustrated by Fig. 1, crosslinked PEG remains on the surface while uncrosslinked PEG is washed off by de-ionized water.

Results: -The hydration of PEG gel is noted to be one of the main reasons for its anti-fouling behavior. We can

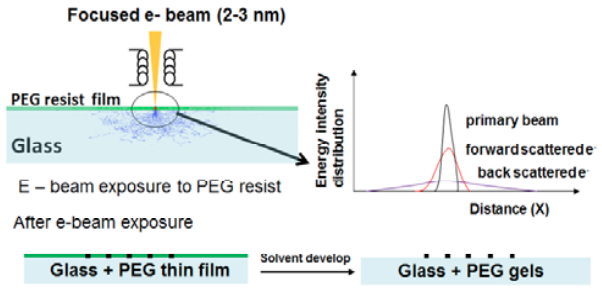

Fig. 1 – Schematic illustration of the e-beam PEG patterning process.

control the swelling of patterned PEG gels and, hence, their protein-repulsive properties by applying different beam dose and energies. However, as illustrated in Fig. 1 (right inset), the incident, forward-scattered, and back-scattered electrons can deposit energy in the PEG film, with various degrees of delocalization and dose. Confocal fluorescence imaging (Fig. 2) showed that the spatial distribution of surface-adsorbed fibronectin illustrates these effects for 2 keV and 30 keV incident electrons with point doses ranging from 1 ~ 1000 fC. Green region

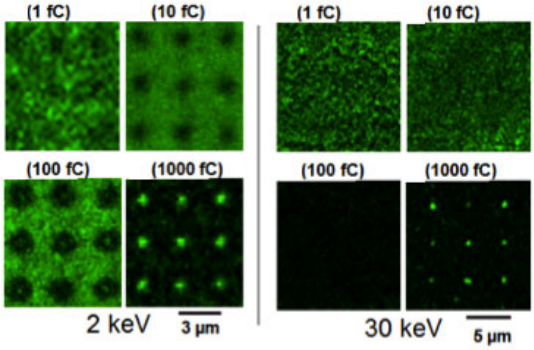

Fig. 2 – laterally modulated fibronectin adsorption depends on the incident electron energy and dose used to pattern PEG.

represent surfaces covered by Fn and black region represent single layer (with several nanometres thickness measured by AFM) of PEG molecules crosslinked by backscattered electrons which can repel Fn adsorption. The fine-scale lateral modulation of surface adhesiveness can be used to differentially control the surface adhesion by osteoblasts and by bacteria. Figure 3. illustrates a case where e-beam crosslinked PEG gels have been patterned over 200 x 200 µm areas at an inter-gel spacing of 1 µm. A negligible amount of bacteria adhere under such conditions (~~f~~Fig. 3A) while osteoblasts are able to grow over the cell-repulsive gels and adhere to the cell-adhesive silicon in between (~~f~~Fig. 3B).

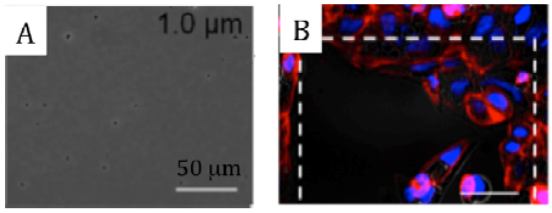

Fig. 3 – PEG gels spaced 1 mm apart repel S. epidermidis bacteria (A) while still enable U2OS pre-osteoblasts to adhere (B).

Conclusions: The specific nature of how surface patterning of PEG gels depends on incident electron energy and dose is a complex process but must be controlled in order to control gel properties. –However, the sub-micron scale precision for surface patterning afforded by e-beam processes can identify new regimes to differentially control cell/bacteria surface interactions.